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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
EWOLDT, GERALD R	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 01/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/155,590	SCHLOM ET AL.	
	Examiner	Art Unit	
	G. R. Ewoldt, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *06 October 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-25,27,32-34,66-68 and 70* is/are pending in the application.

4a) Of the above claim(s) *16-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *10-15,25,27,32-34,66-68 and 70* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 10-15, 25, 27, 32-34, 66-68, and 70 are being acted upon.

2. In view of Applicant's amendment and remarks, filed 10/06/03, the previous rejection under the second paragraph of 35 U.S.C. 112 has been withdrawn. Additionally, the objection to the specification has been withdrawn.

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 10-15, 27, and 32 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Van Elsas et al. (1995) or Gjertsen et al. (1996) in view of Ruppert et al. or U.S. Patent No. 5,861,372 (1999), for the reasons of record as set forth in Papers No. 16, 23, and 35, mailed 10/11/01, 1/14/02, and 6/05/03, respectively.

As set forth previously,

"Van Elsa et al. teaches a mutant *ras* peptide of about 10 or 13 amino acids in a pharmaceutically acceptable carrier comprising the sequence KLVVVGADGV (see particularly page 391, Table I), that binds human MHC HLA-A and thus would be inherently capable of eliciting $CD8^+$ lymphocytes. Note that "eliciting" a lymphocyte is an indefinite recitation, however, for examination purposes the term is considered to mean eliciting a $CD8^+$ response."

"Gjertsen et al. teaches a mutant *ras* peptide of about 10 or 13 amino acids comprising the sequence KLVVVGADGVGKSALTI (see particularly page 451, Table I and Table III), that binds MHC HLA-A and elicits $CD8^+$ lymphocytes. Note that "eliciting" a lymphocyte is an indefinite recitation, however, for examination purposes the term is considered to mean eliciting a $CD8^+$ response."

"Van Elsa et al. and Gjertsen et al. differ from the claimed invention in that the peptides taught by the references differ from the claimed peptide species in that the reference peptides begin with an N-terminus K while on the claimed peptide the

mutant *ras* N-terminus K has been replaced with a Y."

"Ruppert et al. teaches that the addition or replacement of an N-terminus amino acid residue with a Y improves binding of a peptide to HLA-A2 (see particularly page 932, Figure 3)."

"The '372 patent teaches that Y can be added to peptide fragments to facilitate the addition of detectable labels to said fragments (see particularly column 22, lines 25-28)."

"From the teachings of the references it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to replace an N-terminus K, on the mutant *ras* peptide taught by Van Elsa et al. or Gjertsen et al., with an N-terminus Y, as taught by Ruppert et al. or the '372 patent. One of ordinary skill in the art would have been motivated to make said change to facilitate either better HLA-A2 binding, as taught by Ruppert et al., or to facilitate labeling, as taught by the '372 patent."

Applicant's arguments, filed 10/06/03 have been fully considered but they are not persuasive. Applicant argues "Van Elsas et al. provide p21ras-derived peptides of 9 and 11 mer in size (see Van Elsas et al. page 391 Table 1) and experiments to bind of the peptides [sic] to HLA-A*0201. Van Elsas et al. failed to induce CTL using 9 mer peptides (see Van Elsas et al. page 394 column 1, describing "not yet been able to induce responses").

It is unclear to the Examiner how an out of context quote supports Applicant's arguments. Applicant is advised that the reference actually indicates that wild-type sequences, as opposed to the mutant sequences of the reference and the instant claims, had "not yet been able to induce responses".

Applicant argues "Gjertsen et al. provide a number of 17 mer peptides (see Gjertsen et al. Table I on page 451), however, experimental findings would not (see Gjertsen et al. Tables II-IV on pages 451-452) motivate others to use the disclosed peptides because the authors specifically indicated in conclusion that "the study [] do not allow any conclusions regarding the tumour response to ras peptide vaccination" (see Gjertsen et al. page 452, right column, conclusion paragraph 3). Therefore, Gjertsen et al. provide no incentive to the skilled artisan to rely upon its techniques."

Again Applicant has provided a quote from the reference that is at best incomplete. The authors indicate that the of 5 peptide-treated patients, 2 generated an immune response and 3 experienced pain relief. The reason that no conclusions could be

drawn was that the experimental group was too small to derive statistically significant results. This seems to be a curious line of argument and it is unclear to the Examiner why Applicant would adopt it. Applicant's position appears to be that even though the reference teaches an *in vivo* response rate of 100%, i.e., *all* of the patients experienced at least some relief, Applicant believes that this is insignificant. Yet, Applicant provides just marginal *in vitro* T cell proliferative data in support of the instant invention. It would seem then that if the results of the reference must be considered to be insignificant, then the data of the instant specification (none of which have been established to be scientifically significant) could not be considered enabling.

Applicant argues "Moreover, as indicated above, Gjertsen et al. used 17 mer peptides (see Gjertsen et al. Table I on page 451), in contrast, according to the invention, mutant ras peptides of the present invention "having a size of 8 to 13 amino acids" (see, for example, specification WO 97/40156 A1, page 10 lines 1-2). Thus, the size of the peptides of the instant invention is over 20% smaller than the peptides disclosed by Gjertsen et al.".

Applicant is advised that the recitation of "peptide having a size of 8 to 13 amino acids, comprising," which includes *two* open modifiers (having and comprising) provides no limitation to the size of the peptides of the instant claims except a minimum length of 8 amino acids.

It remains the Examiner's position the rejection is based on either of two primary references in which the claimed peptide, differing only by the absence an N-terminus tyrosine, is taught. The secondary references provide two separate reasons for modifying the peptides of the primary references by the inclusion of an N-terminus tyrosine. Accordingly, the peptide of the instant claims is obvious and the rejection is maintained.

5. Claims 25 and 66-67 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Van Elsas et al. (1995) or Gjertsen et al. (1996) in view of Ruppert et al. or U.S. Patent No. 5,861,372 (1999) as applied to claims 10-15, 27, and 32 above, and further in view of U.S. Patent No. 6,039,948 (2000), for the reasons of record as set forth in Papers No. 16, 23, and 35, mailed 10/11/01, 1/14/02, and 6/05/03, respectively.

Applicant's arguments, filed 10/06/03, have been fully considered but they are not persuasive. Applicant argues that the additional reference does not rectify the deficiencies of the primary references of Van Elsas et al., Gjertsen et al.

See the Examiner's arguments regarding the aforementioned assertions in Section 4, above.

6. Claims 33, 68 and 70 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Van Elsas et al. (1995) or Gjertsen et al. (1996) in view of Ruppert et al. or U.S. Patent No. 5,861,372 (1999) as applied to claims 10-15, 27, and 32 above, and further in view of U.S. Patent No. 5,800,810 (1998), for the reasons of record as set forth in Papers No. 16, 23, and 35, mailed 10/11/01, 1/14/02, and 6/05/03, respectively.

Applicant's arguments, filed 10/06/03, have been fully considered but they are not persuasive. Applicant argues that the additional reference does not rectify the deficiencies of the primary references of Van Elsas et al., Gjertsen et al.

See the Examiner's arguments regarding the aforementioned assertions in Section 4, above.

7. Claim 34 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Van Elsas et al. (1995) or Gjertsen et al. (1996) in view of Ruppert et al. or U.S. Patent No. 5,861,372 (1999) as applied to claims 10-15, 27, and 32-33 above, and further in view of U.S. Patent No. 6,001,349 (1999), for the reasons of record as set forth in Papers No. 16, 23, and 35, mailed 10/11/01, 1/14/02, and 6/05/03, respectively.

Applicant's arguments, filed 10/06/03, have been fully considered but they are not persuasive. Applicant argues that the additional reference does not rectify the deficiencies of the primary references of Van Elsas et al., Gjertsen et al.

See the Examiner's arguments regarding the aforementioned assertions in Section 4, above.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 10-15, 25, 27, 32-34, 66-68, and 70 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

a mutant *ras* peptide consisting of the sequence YLVVVGADGV, does not reasonably provide enablement for:

a mutant *ras* peptide comprising (or having) the sequence YLVVVGADGV, for the reasons of record set forth in Paper No. 35, mailed 6/05/03.

Applicant's arguments, filed 10/06/03, have been fully considered but they are not persuasive. Applicant argues "applicants point out that the new ground of rejection is moot in view of currently amended claim 10, which recites "A mutant ras peptide having a size of 8 to 13 amino acids.".

As set forth above, Applicant is again advised that the recitation of "peptide having a size of 8 to 13 amino acids, comprising," which includes *two* open modifiers (having and comprising) provides no limitation to the size of the peptides of the instant claims except a minimum size of 8 amino acids. Thus, Applicant has not addressed the rejection as it pertains to peptides other than those 8-10 amino acids in length.

10. The following are new grounds of rejection necessitated by Applicant's amendment.

11. Claims 10-15, 25, 27, 32-34, 66-68, and 70 is rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically: "A mutant *ras* peptide <u>having a size of 8 to 13 amino acids</u>".

Applicant indicates that the specification supports the newly amended claims at page 10, lines 1-2. Applicant is advised that the specification discloses only a peptide "between about 8 to 13 amino acids", which is not the same as "having a size of 8 to 13 amino acids".

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 10-15, 25, 27, 32-34, 66-68, and 70 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the recitation of a peptide having a size of 8-13 amino acids comprising SEQ ID NO:14 encompasses nonsensical embodiments as it would be impossible to have 8 or 9 amino acid peptides comprising 10 amino acid SEQ ID NO:14.

14. No claim is allowed.

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (703) 308-9805 The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703)

308-3973.

Please Note: inquiries of a general nature or relating to the status of this application should not be directed to the Examiner but rather should be directed to the Technology Center 1600 Customer Service Center at (703) 308-0198.

G.R. Ewoldt, Ph.D.
Primary Examiner
Technology Center 1600

12/23/08
G.R. EWOLDT, PH.D.
PRIMARY EXAMINER